REMARKS

Reconsideration of this application is requested. Claims 1-22 are in the case.

I. CLAIM OBJECTIONS

Claims 1 and 14 have been objected to in view of the expression "fibrinogen containing precipitate". In response, those two claims have been amended to replace that language with "precipitate containing fibrinogen".

II. THE ANTICIPATION REJECTION

Claims 1-5, 7-12, 17 and 18 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent 4,789,733 to Winkelman. That rejection is respectfully traversed.

The present invention is based on the finding that a heparin precipitate containing fibrinogen can be resolubilized with a solution containing at least 0.1 M salt to provide a fibrinogen preparation of high specific activity. The claims of the present application include the following essential features:

(i) adding an effective amount of sulphated polysaccharide (SPS) to a 'fibrinogen containing solution to form a fibrinogen containing precipitate; and

(ii) extracting fibrinogen from the fibrinogen containing precipitate from step (i) with a solution containing at least 0.1 M, and preferably at least 0.2 M, salt to obtain a fibrinogen enriched preparation.

Winkelman does not disclose a method which involves both of these steps. In

particular, Winkelman does not disclose a method which involves extracting fibrinogen from a fibrinogen containing precipitate using a solution containing at least 0.1 M salt. Rather, saline solution is used in the Winkelman method to precipitate Factor VIII and fibrinogen from a supernatant.

The Examiner refers to Example 23 of the Winkelman patent which describes:

(1) extracting proteins from cryoprecipitate using heparin and aprotinin;

(2) precipitating fibrinogen and fibronectin by adjusting the pH to 6.3 and reducing temperature;

(3) recovering the supernatant and precipitating the Factor VIII (and remaining fibrinogen) using saline; and

(4) re-dissolving the precipitate (containing fibrinogen as well) in a Tris/citrate/chloride buffer solution.

This method differs substantially from the present invention in that it is unclear in Example 23, step (2) what causes the fibrinogen and fibronectin to precipitate. In particular, it is unclear whether precipitation is effected by the change in pH, or the presence of the heparin, aprotinin (cACA), or the citrate buffer from step 1. In other words, there is no disclosure of the addition of an "effective amount of sulphated polysaccharide" to effect precipitation as required by the present claim 1. In addition, there is no disclosure (or suggestion) of extracting fibrinogen using a solution containing at least 0.1 M, and preferably at least O.2M salt. Indeed, Example 23 of Winkelman uses salt solution (saline) to precipitate Factor Viii and fibrinogen and in this sense, leads **away** from the present invention.

The Examiner also refers to Example 24 of the Winkelman patent where it is clear that heparin is used to precipitate the fibrinogen/fibronectin. Once again, it is the supernatant from this precipitation that is used in further processing. Example 24 does not describe the step of extracting fibrinogen from a precipitate using at least 0.1 M salt solution.

In light of the above, it is clear that Winkelman does not anticipate the presently claimed invention. Reconsideration and withdrawal of the outstanding anticipation rejection based on that reference are accordingly respectfully requested.

III. THE OBVIOUSNESS REJECTION

Claims 1-20 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Winkelman in view of Mosesson and Alteri et al (US 20020131970 A1). That rejection is respectfully traversed.

Winkelman is irrelevant to the claimed invention for the reasons discussed above. The deficiencies of Winkelman are not cured by Mosesson and Alteri. Mosesson describes the use of eACA and lysine to change the solubility of fibrinogen and plasminogen. The precipitate used was an ethanol/salt precipitate, not a Heparin precipitate, as required in the present claims. Winkelman describes the extraction of a Factor VIII precipitate that contains fibrinogen using an ill-defined Tris/citrate/chloride buffer. Protein solubility characteristics strongly depend on the protein compositions, the presence of different proteins, the protein concentration, as well as the ionic strength and the dielectric constant of water. That being so, a person of ordinary skill would not be able to predict, from combining both Mosesson and Winkelman, the buffer

required to resolubilize fibrinogen from a precipitate containing heparin, plasminogen and very little Factor VIII. It has only been through considerable effort and ingenuity that the present inventors have found that at least 0.1 M salt and eACA result to significant recovery of fibrinogen from Winkelman's heparin precipitate, a precipitate that has been discarded in the past.

Alteri describes the purification of fibrinogen by way of dissolution of an alcohol precipitate using 0 55 M Tris/citrate/chloride butter at pH 6 5, reprecipitation with ethanol and then affinity chromatography. There is no disclosure or suggestion of how to redissolve this second precipitate. If the person of ordinary skill turns to Winkelman to find out how to redissolve fibrinogen, that person will attempt to use a Tris based-buffer, of undefined concentration and pH.

In light of the above, it is clear that the combination relied upon by the Examiner does not disclose or suggest the method of precipitating fibrinogen using heparin and a subsequent extraction of fibrinogen from the heparin precipitate using a salt of concentration at least 0.1 M. A person of ordinary skill would not, therefore, have been motivated to arrive at the presently claimed invention based on the combined disclosures of Winkelman, Mosesson and Alteri. Absent any such motivation, a *prima facie* case of obviousness is not generated in this case. Reconsideration and withdrawal of the outstanding obviousness rejection are accordingly respectfully requested.

Allowance of the application is awaited.

Respectfully submitted,

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